

Rapid Response Fact Sheet

The Rapid Response Team (RRT) was created in November of 2000, as part of the reengineering of the Office of Testing and Research (OTR). The RRT is a composed of a group of multidisciplinary scientists from the Office of Pharmaceutical Sciences, including OTR, ONDC, OCPB and OGD. The group is directly under the Office of Pharmaceutical Sciences (OPS). The primary function of the RRT is to provide timely and specific research support (laboratory-based or literature-based) for designated regulatory issues that require further agency study. The RRT responds to well-defined scientific questions that are raised by CDER review divisions. The goal is to provide the review divisions with sound scientific data, or literature, which will be used in the regulatory process. The projects that are accepted by the RRT are expected to have a short turnaround time, because they are given high priority and are considered to be PDUFA activities. Following the completion of a Rapid Response Project, a report is written and made available to the review division. The RRT reports are expected to serve as consults to the review division.

Accomplishments:

The following is a list of some of the projects that the RRT has completed to date:

1. Determination of the bioequivalence of generic versions of cyclosporin versus the innovator product. Response time 4 months.
2. Dissolution properties of levothyroxine tablets. Response time 2 weeks.
3. Providing OGD with information on Imipramine biopharmaceutical classification standards. Response time 2 months.
4. Providing information on whether a chemical or assay or a bioassay for Urofollitropin needed to be conducted by the sponsor, determination of bioequivalence. Response time 3 weeks.
5. Doxycycline Hyclate tablet palatability study in human subjects, to identify dosing regimens that would be appropriate for pediatric populations in the event of a bioterrorism incident. Response time 3 weeks.
6. Potassium Iodide tablet palatability study in human subjects, to identify dosing regimens that would be appropriate for pediatric populations in the event of a bioterrorism incident. Response time 2 months.
7. Permeability study of commercially available gloves to lindane lotion and shampoo

Ongoing projects:

1. Assessing the neurotoxicity of ketamine in juvenile animals in order to extrapolate to pediatric populations currently dosed with ketamine for setting of broken bones. This project is ongoing and has been nominated to the NTP (National Toxicology Program) for further evaluation in primates.

2. Ciprofloxacin tablet palatability and bioequivalence study in human subjects.
3. Neurotoxicity of Accutane in a rodent model.
4. BCS classification, dissolution and potency of commercially available levothyroxine drug products.

Not all the completed or currently ongoing projects have been described in the list above.

In-House capabilities:

OTR Capabilities and Expertise

Division	Expertise	Lab. Equipment
Laboratory of Clinical Pharmacology (LCP, Mod 1 and NLRC)	<ul style="list-style-type: none">• Analysis of drugs in biological fluids• Use of human liver tissue for pharmacological studies in vitro• Application of Pharmacokinetics to metabolism and drug-drug interactions• Assessment of reactive metabolites as potential hepatotoxins• Characterization of imaging targets as biomarkers	HPLC (several detectors), LC-MS-MS, GC, GC-MS, Radiochemical detectors
Division of Pharmaceutical Analysis (DPA, St. Louis and Mod 1)	<ul style="list-style-type: none">• Characterization of Reference Standards• Evaluation and Validation of Regulatory Analytical Methods• Analytical Method Development• Forensic and Counterfeit Evaluation• Compliance Investigations	GC (FID, TC, EC, Flame Photometric, MS detectors), HPLC (MS, MS/MS, Fluorescence, UV/VIS, RI, PDA, IC detectors), Capillary Electrophoresis, TLC, IR, NIR, UV/VIS, Thermal (TGA/DSC), Titrators, Dissolution apparatus, Particle sizing. In addition, personnel are on staff with experience in NMR, Raman, Fluorescence and Chemometrics.
Division of Product Quality Research (DPQR)	<ul style="list-style-type: none">• In Vitro Drug Permeability• Analytical Method Development• Solid State Characterization• Shelf Life Stability Studies• Dissolution• Botanicals	Stability Chambers, GC, HPLC, Dissolution apparatus, Capillary Electrophoresis, HPLC (UV, VIS, Fluorescence,), Scintillation Counter, Titrators, Spectrophotometers (UV, NIR), Thermal (TGA, DSC). In addition, personnel are on staff with experience in NMR, NIR Imaging and Chemometrics, Cell culture capabilities.
Division of Applied Pharmacology Research (DAPR)	<ul style="list-style-type: none">• Whole Animal Studies• Molecular Biology (PCR, DNA Sequencing, Oligonucleotide Synthesis, Gel Electrophoresis, Gene Typing/Gene Expression analysis, Image analysis• Biochemistry (Enzyme assay, Western blotting)• Clinical chemistry and Immunology (ELISA, Flow cytometry, cell culture)• Biomarker identification• Cytogenetics	Animal facility, High Throughput Sequence detection system, Oligonucleotide DNA Synthesizer, Electrophoresis, Cameras, darkroom facilities and imaging software, Flow Cytometer, cell sorter, Cell culture equipment, Zeiss Photomicroscope,

Available funds:

Funds for appropriate research projects are made available by OPS.

Standard format for RRT proposals:

The following information needs to be available to RRT prior to initiation of a project:

1. Title of project
2. Introduction/Relevance to FDA and public health impact
3. Questions that the study will address
4. Expectations from the Rapid Response Team
5. Anticipated regulatory outcome (how will be information generated be used)
6. Expected time frame for completion of the project

Process for requesting RRT involvement:

The formal process is as follows:

1. The sponsor of a project provides RRT member with information to complete the above listed format. This will constitute a Draft proposal. All potential projects, whether accepted by RRT or not deemed appropriate, need to have a Draft Proposal submitted to RRT.
2. The draft proposal is discussed at the RRT meeting for review.
3. The RRT decides on the appropriateness of the draft proposal and responds to the sponsor of the proposal in a timely manner.
4. The RRT will collaborate with the sponsor to write a detailed proposal that will serve as the basis for the study design
5. The RRT will carry out the study
6. The RRT will write the report and submit it to the sponsor

Rapid Response Members:

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